REMARKS

This communication is being filed in response to the Office Action dated October 23, 2003. Claims 13-21 are pending. Claim 21 is rejected under the second paragraph of 35 U.S.C. § 112 as being indefinite. Claims 13-15 and 19 are rejected under 35 U.S.C. § 102(b) as being anticipated by Giles (U.S. Patent No. 4,603,141) and Applicants' alleged acknowledgement in the instant specification (p. 6, lines 8-11). Claim 13 is rejected under 35 U.S.C. § 102(b) as being anticipated by Scheurer *et al.* (Am. J. Physiol. 1997;272:R2017-2024) and Applicants' alleged acknowledgement in the instant specification (p. 6, lines 12-16). Claim 18 is rejected under 35 U.S.C. § 102(b) as being anticipated by Beale (U.S. Patent No. 5,756,469). Claims 19-20 are rejected under 35 U.S.C. § 103(a) as being rendered obvious by Giles (U.S. Patent No. 4,603,141). Claims 16 and 17 are objected to as being dependent upon a rejected base claim, but are otherwise in condition for allowance, while Claim 21 is objected to for being grammatically incorrect.

Applicants herein have amended Claims 13, 14, 18, 19 and 21. Applicants also have added Claims 22-26. Support for the amendments may be found in the instant specification, at, *inter alia*, the first paragraph of page 1, the last paragraph of page 5 through the first paragraph of page 8, and the last paragraph of page 11 through the first paragraph of page 12. Support for the new claims also may be found in the instant specification at the last paragraph of page 11 through the first paragraph of page 12. Applicants therefore submit that the changes to the claims do not constitute the introduction of new matter. In light of these amendments, and for the reasons set forth below, Applicants respectfully traverse the Examiner's rejections of the claims of the instant application.

I. The Claims Are Grammatically Correct

The Examiner objects to Claim 21 as being grammatically incorrect. Specifically, the

Examiner notes that Claim 21, as originally filed, lacked a form of the verb "administer." Applicants hereinabove have amended Claim 21 so that it is now directed toward a method for treatment of heart failure "which comprises administering... a cortisol antagonist." Applicants submit that Claim 21 is now grammatically correct and respectfully request withdrawal of this objection to the pending claims.

II. The Claims Are Definite

Claim 21 is rejected under the second paragraph of 35 U.S.C. § 112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. The Examiner alleges that Claim 21 is indefinite in its recitation of the phrase "the daily dosage," because Claim 18, from which Claim 21 had depended, did not explicitly provide antecedent basis for this phrase. The Examiner also contends that Claim 21 is broader in scope than Claim 18 because the term "a subject" in Claim 21 is broader than the term "a mammalian subject" in Claim 18.

In response, Applicants have amended Claim 21 as indicated hereinabove. As amended, Claim 21 now depends from Claim 19, which also has been amended to provide explicit antecedent basis for the phrase "the daily dosage" in Claim 21. Claim 21 also has been amended so that the phrase "the subject" replaces the phrase "a subject." In light of these amendments, Applicants respectfully request withdrawal of the rejection of Claim 21 under the second paragraph of 35 U.S.C. § 112.

III. The Claims Are Not Anticipated

Claims 13-15, 18 and 19 are rejected under 35 U.S.C. § 102(b). Claims 13-15 and 19 are rejected on this basis as being anticipated by Giles (U.S. Patent No. 4,603,141) and Applicants'

acknowledgement in the instant specification (p. 6, lines 8-11). Claim 13 also is rejected under 35 U.S.C. § 102(b) as being anticipated by Scheurer *et al.* (Am. J. Physiol. 1997;272:R2017-2024) and Applicants' acknowledgement in the instant specification (p. 6, lines 12-16). Claim 18 is rejected under 35 U.S.C. § 102(b) as being anticipated by Beale (U.S. Patent No. 5,756,469).

The Examiner contends that Giles teaches the administration of clonidine or salts thereof for the treatment of chronic congestive heart failure and for increasing exercise tolerance in individuals so afflicted, and that Applicants, in lines 8-11 of the first full paragraph on page 6 of the instant specification, acknowledge that clonidine is known to be a cortisol antagonist. Consequently, the Examiner concludes that Giles anticipates Claims 13-15 and 19 of the instant application.

Applicants respectfully disagree with the Examiner's characterization of the teaching of Giles. Applicants submit that Giles merely teaches the use of clonidine as an anti-hypertensive agent to treat chronic congestive heart failure, and makes no reference to clonidine's activity as a cortisol antagonist. For example, Giles explicitly identifies clonidine as an anti-hypertensive agent at column 1, lines 40-44. Furthermore, Giles indicates that

> [b]olus intravenous injections of clonidine HCl have produced decreased sympathetic outflow, increased vagal tone and sensitivity of the baroreceptor reflex, with peak effects occurring at 5-20 minutes. Reductions were observed in heart rate, left ventricular filling pressure (preload), mean systemic arterial pressure (afterload), mean pulmonary artery pressure and right atrial pressure.

All of these actions are compatible with clonidine's role as an α-adrenergic receptor agonist. Therefore, Applicants assert that one of ordinary skill, reading the disclosure of Giles, would understand that it is the anti-hypertensive effects of clonidine that are mediating the changes observed by Giles on cardiac function after clonidine administration and not clonidine's inherent properties as a cortisol antagonist.

However, to further the prosecution of the instant application, and without conceding the correctness of the Examiner's position regarding the teachings of Giles, Applicants have amended Claims 13 and 19 to exclude clonidine from the genus of cortisol antagonists being claimed. In support for these amendments, Applicants note that a genus of cortisol antagonists suitable for use in the instant invention is taught in the specification, beginning at the last paragraph of page 5 and continuing through the first full paragraph on page 8. Applicants further note that, according to § 2173.05(i) of the *Manual of Patent Examining Procedure* ("MPEP"), "[i]f alternative elements are positively recited in the specification, they may be *explicitly excluded* in the claims." (emphasis added). The Court of Customs and Patent Appeals, in *In re Johnson*, 558 F.2d 1008, 1018 (CCPA 1977), stated that "applicants frequently discover during the course of prosecution that only a part of what they invented and originally claimed is patentable. It is for the inventor to decide what bounds of protection he will seek" Thus, in *Johnson*, the court held that the deletion of certain species from protection where the genus encompassing those species had been fully disclosed did not render the application defective under 35 U.S.C. § 112. In support of this holding, the court stated that "[t]he notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, *that genus minus two of those species*, ... appears to result from a hypertechnical application of a legalistic prose resulting from the provision of [35 U.S.C. § 112]." *Id.* at 1019 (emphasis added). Applicants therefore submit that the Claims 13-15 and 19, as presently amended, are not anticipated by Giles, and respectfully request that the Examiner withdraw the rejections of these claims under 35 U.S.C. § 102(b).

The Examiner contends that Scheurer *et al.* teach that the administration of mifepristone reduces a cardiac pathology (infarct size) in a mammal (corticosterone-treated rats). The Examiner

therefore asserts that Scheurer *et al.* anticipate Claim 13 of the instant invention. In response, Applicants note that Claim 13, as presently amended, is directed toward heart failure rather than cardiac pathology. Because infarct size is not a form of heart failure, as defined in the third full paragraph on page 3 of the specification, Applicants submit that amended Claim 13 is not anticipated by Scheurer *et al.* Applicants respectfully request that the rejection of Claim 13 under 35 U.S.C. § 102(b) as being anticipated by Scheurer *et al.* be withdrawn.

The Examiner asserts that Beale teaches a composition comprising a cortisol blocker (a "cortisol antagonist") and pyruvate (a "second drug"), thereby anticipating Claim 18 of the instant application. Applicants note that, as presently amended, Claim 18 is directed toward a composition comprising ketoconazole or a derivative thereof, rather than a cortisol antagonist. Because Beale does not teach a composition comprising ketoconazole or derivatives thereof, Applicants submit that Beale no longer anticipates the pending claims. Accordingly, Applicants respectfully request that the rejection of Claim 18 under 35 U.S.C. § 102(b) be withdrawn.

IV. The Claims are Not Obvious

Claims 19-20 are rejected under 35 U.S.C. § 103(a) as being rendered obvious by Giles (U.S. Patent No. 4,603,141). According to the Examiner, the only difference between the teachings of Giles and the subject matter of Claims 19-20 is that Giles highlights exercise intolerance as a symptom of congestive heart failure while Claims 19-20 list additional symptoms that the Examiner contends would be obvious to one of ordinary skill in the art.

Applicants respectfully submit that Giles cannot render obvious Claims 19-20, as presently amended, because Giles does not teach or suggest the use of cortisol antagonists other than clonidine for the treatment of heart failure. Applicants further submit that one of ordinary skill, faced with the

disclosure of Giles, would not be motivated to combine Giles with other teachings that disclose clonidine as a cortisol antagonist, because Giles makes it abundantly clear that the beneficial effects of clonidine disclosed therein are the result of the actions of clonidine on the sympathetic/parasympathetic nervous system axis. For example, Giles notes that "[c]hronic congestive heart failure (CHF) is associated with increased activity of the sympathetic nervous system[,]" Giles, column 1, lines 12-13, and that "intravenous injections of clonidine HCl have produced decreased sympathetic outflow, increased vagal tone and sensitivity of the baroreceptor reflex[,]" Giles, column 1, lines 53-55, all indicators that clonidine is acting as an α-adrenergic agonist rather than a cortisol antagonist. Thus, one of ordinary skill in the art, if at all motivated to modify the teachings of Giles, would do so by examining other α-adrenergic agonists or other agents that affect the sympathetic/parasympathetic nervous system axis, but would not be motivated to consider agents that exert no effect on the sympathetic or parasympathetic nervous systems. Applicants therefore submit that Giles does not render obvious Claims 19-20 of the instant application as presently amended, and respectfully request that the Examiner withdraw the rejection of these claims under 35 U.S.C. § 103(a).

CONCLUSION

Based on the foregoing remarks and in light of the amendments, Applicants submit that the present application is in condition for allowance. A Notice of Allowance is therefore respectfully requested.

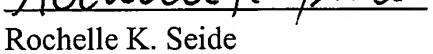
Applicants believe a fee of $950.00 is due with this response, representing the fee required under 37 C.F.R. § 1.17(a)(3) for a three-month extension for a non-small entity. A check in that amount is enclosed. Should any additional fees be required in connection with this filing, or should

any overpayment have been made, the Commissioner is hereby authorized to charge any additional fees or credit any overpayments to Deposit Account Number 02-4377. Two copies of this communication are enclosed.

If a telephone interview would be of assistance in advancing the prosecution of the subject application, Applicants' undersigned attorney invites the Examiner to telephone at the number provided below.

Respectfully submitted,

BAKER BOTTS L.L.P.



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